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IP

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/260,037	03/02/99	YACOBY-ZEEVI	0 910/13

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EXAMINER

HUTSON, R

ART UNIT

PAPER NUMBER

1652

DATE MAILED:

08/01/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.  
**09/260,037**

Applicant  
**Yacoby-Zeevi**

Examiner  
**Richard Hutson**

Group Art Unit  
**1652**



☒ Responsive to communication(s) filed on May 18, 2000

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11, 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claim

☒ Claim(s) 1-53 is/are pending in the application

Of the above, claim(s) 9-53 is/are withdrawn from consideration

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 1-8 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☒ None of the CERTIFIED copies of the priority documents have been  
☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

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### DETAILED ACTION

Claims 1-53 are pending.

Claims 9-53 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 4.

Claim 1 has been amended.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Fuks et al. (US Pat No: 5,362,641).

The rejection is stated in the previous office action. As discussed in the previous office action, Fuks et al. teach a substantially purified heparanase from human SK-HEP-1 cell line, methods of purifying the heparanase and the use of this heparanase as the basis for a pharmaceutical composition useful for the enhancement of the wound-healing process.

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The amendment of claim 1 to recite “for use in vivo” and “so as to enhance extravasation of said biological material in vivo” are intended “uses” of the biological preparation and therefore carry no patentable weight.

Applicants traverse this rejection on the basis rejection that the Fuks et al. patent does not anticipate a biological preparation comprising a biological material and a purified, natural or recombinant, extracellular matrix degrading enzyme being externally adhered thereto.

Applicants suggest that “Fuks et al. teach the use of heparanase as a pharmaceutically active ingredient occluded within drug delivery systems” contrary to the instant invention which teaches use of an enzyme such as heparanase externally adhered to a biological material. This argument is not held persuasive, for a number of reasons.

First, the specification teaches that the terms “externally adhered” refers to “associated with” (page 31, line 5) and Fuks et al. clearly meets the limitation of the claim drawn to a biological preparation comprising a biological material and an extracellular matrix degrading enzyme “associated with” said material.

Second, as discussed in the previous office action, Fuks et al. teach the use of this heparanase as the basis for a pharmaceutical composition comprising the heparanase in combination with a pharmaceutically acceptable, preferably slow releasing carrier. Fuks et al.’s invention is not limited to this singular mode of administration. Fuks et al. also teach the use of therapeutically useful heparanase preparations combined with pharmaceutically carriers in the form of lotions, ointments, powders, or any other appropriate vehicle of application. One of skill

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in the art know that lotions are intended for external application, thus application of said lotions, ointments or powders containing heparanase preparations would result in a biological material and said heparanase preparation externally adhered to.

Therefore claims 1 and 6 remain anticipated by Fuks et al.

Claims 1, 2, 4 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by the Sigma Catalog (page 275, 1992).

The rejection is stated in the previous office action. As discussed, Sigma sells and teaches the use of collagenase for the hydrolysis of native collagen in the isolation of cells from animal tissue and tissue culture.

Applicants traverse this rejection on the basis that the intended use of the Sigma preparation is for the dissociation of cells in a biological sample and this is in contrast to the intended use of the instant invention. This argument is not held persuasive, because as discussed above the applicants amendment of claim 1 to recite “for use in vivo” and “so as to enhance extravasation of said biological material in vivo”, being intended “uses” of the biological preparation therefore carry no patentable weight.

Therefore, claims 1, 2, 4 and 7 remain anticipated by the Sigma Catalog.

### ***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

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Claims 1-5, 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fuks et al. and Wang et al. (J. Orthop. Res., 14 (2): 149-153 1996, abstract).

This rejection is stated in the previous office action.

Applicants traverse this rejection on the basis that the present invention uses the extracellular matrix degrading activity of heparanase so as to assist extravasation of a biological material within the body, not through a secondary effect of releasing factors from the extracellular matrix.

As discussed in the previous office action, one of ordinary skill in the art at the time of filing would have been motivated to pretreat bone grafts prior to implantation of the grafts in recipient bone tissue with a growth factor to stimulate integration of the graft into the recipient tissue as taught by Wang et al. Based on the teaching of Fuks et al. one of ordinary skill in the art at the time of filing would have been motivated to treat said bone grafts with heparanase as opposed to basic fibroblast growth factor in order to stimulate the release of endogenous FGF from the recipient tissue. Since the instant claims are to the biological preparation, and not to the method of use, the mechanism of action of heparanase preparation and hence the motivation for the claimed biological preparation carries no patentable weight thus applicants argument is not held persuasive.

Applicants further traverse the rejection on the basis that both Fuks et al. and Wang et al. fail to teach or suggest a biological material to which heparanase is "externally adhered". As discussed above under 102 rejection, Fuks et al. does teach a biological preparation to which

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heparanase is “externally adhered” to. Further as discussed in the previous office action, one would have been motivated to pretreat bone grafts with heparanase for the reasons of record, thus making obvious a biological preparation comprising a biological material and a purified, natural or recombinant, extracellular matrix degrading enzyme being “externally adhered” thereto.

Therefore, claims 1-5, 7 and 8 remain obvious by Fuks et al and Wang et al.

Claims 3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sigma Catalog.

The rejection is stated in the previous office action. As discussed, Sigma sells and teaches the use of collagenase for the hydrolysis of native collagen in the isolation of cells from animal tissue and tissue culture.

Applicants traverse this rejection, as above, on the basis that the intended use of the Sigma preparation is for the dissociation of cells in a biological sample and this is in contrast to the intended use of the instant invention. As stated above under 102 rejection, this argument is not held persuasive, because as discussed above the applicants amendment of claim 1 to recite “for use in vivo” and “so as to enhance extravasation of said biological material in vivo”, being intended “uses” of the biological preparation carry no patentable weight.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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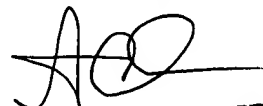
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on M-F from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapy Achutamurthy (Murthy), can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson Ph.D.  
7/25/2000

  
PONNATHAPU ACHUTAMURTHY  
SUPERVISORY PATENT EXAMINER  
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